

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 358-417 are pending in the application, with claims 358 and 411 being the independent claims. Claims 1-357 were previously canceled without prejudice to or disclaimer of the subject matter recited therein. Claims 358, 361-379, 392-395, 401, and 411 are sought to be amended. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Claims 361-379, 392-395, 401, and 411 have been amended to more distinctly claim Applicants' invention. Specifically, claims 358 and 411 have been amended to delete the phrase "which operably encodes" in part (a) and substitute it with the phrase "wherein the polynucleotide expresses." Support for this amendment can be found in the specification as filed, *inter alia*, at page 64, paragraph 0159, to page 66, paragraph 0164. For grammatical correctness, part (b) of claims 358 and 411 has also been amended to insert the word "and" immediately preceding the second "wherein" clause recited in these claims.

Claims 361-379 have been amended to insert the phrase "grams per mole" after the term "MW" (molecular weight) to provide units for each recited molecular weight, as suggested by the Examiner. Applicants respectfully note that addition of the units "grams per mole" is unnecessary because one of skill in the art would recognize that the molecular weight of a substance is typically expressed in units of grams per mole. However, to expedite prosecution, Applicants have amended claims 361-379 as suggested by the Examiner to incorporate units for the specific molecular weights recited in these claims.

Claim 371 has been amended to insert "(w/v) of" immediately after "4%." Support for this amendment can be found in the specification as filed at page 37, paragraph 0096, lines 38-39 (as amended in Applicants' Amendment and Reply Under 37 C.F.R. § 1.111, filed on December 23, 2002), and at page 45, paragraph 0107, line 4. For grammatical correctness, claims 371 and 378 have also been amended to insert the word "of" immediately preceding "a poloxamer," at lines 4 and at lines 2, 5, and 6, respectively. Claim 374 has also been amended to delete "about 0.05% (w/v) to about 0.10% (w/v) of a poloxamer having an approximate hydrophobe molecular weight of 3000 grams per mole and an approximate hydrophile weight percentage of 30%;."

Claim 401 has also been amended to delete the words "in spinal cord" in the phrase "spinal canal in spinal cord." Support for this amendment can be found in the specification as filed at page 68, paragraph 0170, line 11. Claims 392-395 have been amended to delete the phrase "analogs and derivatives."

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

***I. The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph***

The Examiner rejects claims 361-379, 392-395, 401, and 411-417 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (Office Action, at page 3.)

Specifically, the Examiner asserts that claims 361-379 are indefinite because they recite molecular weights but fail to recite units in which the molecular weight is measured. (Office Action, at page 3, lines 4-5.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended claims 361-379 to add the phrase "grams per mole" immediately following each recited molecular weight.

The Examiner also asserts that claim 371 is indefinite because it is allegedly unclear what is intended by "4% a poloxamer," and suggests that "(w/v) of" be inserted in claim 371 after "4%." (Office Action, at page 3, lines 6-7.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended claim 371 as suggested by the Examiner, by inserting "(w/v) of" immediately after "4%" and before "a."

The Examiner further asserts that claims 392-395 are also indefinite because it is allegedly unclear what is intended by the phrase "analogs and derivatives." (Office Action, at page 3, lines 8-14.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended claims 392-395 to delete the phrase "analogs and derivatives."

The Examiner also asserts that claim 401 is indefinite because the claim recites "spinal canal in spinal cord" and this phrase allegedly inverts the relationship between the spinal canal and the spinal cord. The Examiner suggests deleting the word "in" in the phrase "spinal canal in spinal cord" and substituting it with the phrase "surrounding a." (Office Action, at page 3, lines 15-18.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended claim 401 to delete the words "in spinal cord" in the phrase "spinal canal in spinal cord" so that claim 401 recites "spinal canal" as one of the recited cavities. Support for this amendment can be found in the specification, for example, at page 68, in line 11 of paragraph 0170.

Lastly, the Examiner asserts that claims 411-417 are confusing because it is allegedly unclear what composition is being claimed, as claims 411-417, while drawn to a composition, recite method steps that relate to the use of a composition and not to a process of making the composition. The Examiner suggests deleting the phrase "administering into a tissue or cavity of said vertebrate a composition comprising." (Office Action, at page 3, line 19, to page 4, line 2.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended the preamble of claim 411 to delete the phrase "administering into a tissue or cavity of said vertebrate a composition comprising." Because each of claims 412-417 depends from claim 411, it incorporates the limitations of claim 411 and thus the current amendment to claim 411.

Applicants assert that the rejection of claims 361-379, 392-395, 401, and 411-417 under 35 U.S.C. § 112, second paragraph, has been overcome and respectfully request the Examiner to reconsider and withdraw this rejection.

***II. The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph  
(Written Description)***

The Examiner rejects claims 392-395 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. (Office Action, at pages 4 and 5.)

Specifically, the Examiner asserts that the scope of the terms "analogs" and "derivatives" recited in each of claims 392-392 is allegedly unclear because the terms are not defined by the specification, and, further, that "the specification does not describe by structure or reduce to practice any derivatives or analogs" and "fails to provide any relevant identifying characteristics such as known or disclosed correlation between a structure that is required for the recited therapeutic, immunogenic or immunomodulatory functions." (Office Action, at page 4, lines 14-20, and page 5, lines 5-9). The Examiner concludes that "one of skill in the art could not conclude that Applicant was in possession of the claimed genus at the time of filing." (Office Action, at page 5, lines 9-10.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended claims 392-395 to delete the phrase "analogs and derivatives."

Applicants assert that the rejection of claims 392-395 under 35 U.S.C. § 112, first paragraph, has been overcome and respectfully request the Examiner to reconsider and withdraw this rejection.

***III. The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph (Enablement)***

The Examiner rejects claims 358-417 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for methods of and compositions for delivering a polypeptide into a vertebrate by delivery of an RNA virus or DNA that encodes the polypeptide, but lacks transcriptional control sequences in operable association with the polypeptide-encoding sequence. The Examiner states that, accordingly, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. (Office Action, at pages 5-7.)

Specifically, the Examiner asserts that the specification does not define the phrase "operably encodes," and argues that, accordingly, the phrase must be given its broadest reasonable interpretation, which embraces any RNA virus or DNA that encodes a polypeptide, regardless of whether or not it is associated with a promoter. (Office Action, at page 6, lines 8-11.) The Examiner alleges that the specification teaches that non-integrating DNAs are preferred and does not contemplate the use of the invention to integrate any open reading frame downstream of an endogenous promoter, *e.g.*, the specification does not teach how to induce an integrating RNA virus to insert downstream of a promoter such that one can predictably obtain transcription of the desired polypeptide. (Office Action, at page 6, lines 17-22.) The Examiner concludes that one of skill in the art would have to perform undue experimentation to practice the invention commensurate in scope with the claims (Office Action, at page 7, lines 8-10.) The Examiner then suggests that the rejection can be overcome by amending the claims to read "(a) about 1 ng to about 30 mg of a polynucleotide

in aqueous solution wherein the polynucleotide is capable of expressing a polypeptide upon delivery to vertebrate cells". (Office Action, at page 7, lines 11-14.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended part (a) of claims 358 and 411 to read "(a) about 1 ng to about 30 mg of a polynucleotide in aqueous solution, wherein the polynucleotide expresses a polypeptide upon delivery to vertebrate cells *in vivo*;".

Applicants assert that the rejection of claims 358-417 under 35 U.S.C. § 112, first paragraph, has been overcome and respectfully request the Examiner to reconsider and withdraw this rejection.

### ***Conclusion***

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

A handwritten signature in cursive script, appearing to read "Ann E. Summerfield".

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